REMARKS

Claims 42-47, 49-52, 55, 57, 59, 61 and 63 are pending upon entry of the above amendments. Claims 52, 55, 57, 59, 61 and 63 have been amended to recite the full name of "cSNP". Support for the amended claims may be found in the specification, e.g. at page 249, lines 30-31and 427, line 12. No new matter has been introduced. Claim 48 has been canceled. Applicant preserves the rights to pursue the subject matter of claim 48 in a related application.

RESTRICTION REQUIRMENT

The Examiner has withdrawn new claims 48, 53, 54, 56, 58, 60, and 62 which were presented as new claims in Applicant's response to the Restriction Requirement, as not directed to Group II or SEQ ID NO.:38.

Applicant respectfully traverses this action and requests that claims 42-47, 49-52, 55, 57, 59, 61, 63 and 53, 54, 56, 58, 60, 62 be examined together in the instant application .

Group II was defined by the Examiner in the Restriction Requirement dated May 20, 2003 as Claims 5-13, drawn to a nucleic acid, classified in class 536, subclass 23.1. The Examiner further required Applicant to make a sequence election, stating that each sequence is patentably distinct because they are not related sequences. Of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, and 60, Applicant elected SEQ ID NO:38.

The subject matter of claims 53, 54, 56, 58, 60, 62 are sequences reasonably related to SEQ ID NO:38. The only difference between the sequence of SEQ ID NO:38 and each of the sequences claimed in claims 53, 54, 56, 58, 60, and 62 is that the latter contains a single amino acid change at a defined position as compared to the sequence of SEQ ID NO:38. Since SEQ ID NO:38 is a 2,721 amino acid long sequence each of the sequences in claims 53, 54, 56, 58, 60, 62 are 99.97% identical to SEQ ID NO:38. The search of the art relevant to SEQ ID NO:38 will necessarily encompass any sequences known in the art that are 99.97% identical to SEQ ID NO:38, and therefore, no additional burden is placed upon the Examiner to examine the variants presented in claims 53, 54, 56, 58, 60 and 62.

The M.P.E.P. §803 (Eighth Edition, August 2001, revised February 2003) states:

> If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merit, even though it includes claims to independent or distinct inventions.

Applicant submits therefore, that according M.P.E.P. §803.02 claims 42-47, 49-52, 55, 57, 59, 61, 63 and 53, 54, 56, 58, 60, 62 should be examined together because the search and examination of these claims would not unduly burden the Examiner.

Rejections under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 45, 53, 54, 56, 58, 60 and 62 under 35 U.S.C.§112, second paragraph as being indefinite. However, since the Examiner has withdrawn claims 53, 54, 56, 58, 60 and 62 from consideration this rejection is unclear. Applicant is interpreting this as a typographical error, that the Examiner intended to say claims 45, 52, 55, 57, 59, 61, 63. Applicant is responding accordingly. Applicant requests that the Examiner confirm that this interpretation is correct.

Claim 45 has been rejected as the term "complement" is considered to be vague and indefinite by the Examiner. Applicant respectfully disagrees. It is well known in the art that the complement of a first nucleic acid sequence is a matching nucleic acid sequence, in which each base is the matched pair of the base in the corresponding position of the first nucleic acid sequence, the matched pairs being adenine:thymine and guanine:cytosine. (See page 865, Albert L. Lehninger, Biochemistry, Second Edition, Worth Publishers, Inc. New York, NY, 1979) In the specification, at page 199, lines 5-9, it says:

> "In another embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule that is a complement of the nucleotide sequence shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, and 59, or a portion of this nucleotide sequence (*e.g.*, a fragment that can be used as a probe or primer or a fragment encoding a biologically-active portion of an NOVX polypeptide)." Emphasis added.

It is clear that the *complement* of a nucleotide sequence of a specific SEQ ID NO is intended to mean a full length nucleotide sequence comprising the matched base pair at each position of the full length sequence defined by the SEQ ID NO. If anything less than the full length is intended,

the specification specifies a complement of a portion of the nucleotide sequence defined by the SEQ ID NO (or fragment or other appropriate term).

Applicant believes that the Examiner is confusing the definition of "a complement" with the definition of "a complementary" nucleic acid. A *complementary* nucleic acid molecule is referred to as:

> "A nucleic acid molecule that is complementary to the nucleotide sequence shown SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, or 59 is one that is sufficiently complementary to the nucleotide sequence shown SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, or 59 that it can hydrogen bond with little or no mismatches to the nucleotide sequence shown SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, or 59, thereby forming a stable duplex." See instant specification, page 199, lines 9-16.

Thus, a *complementary* nucleic acid sequence may be a full-length complement, or a portion thereof. As such, the use of complement is clear and the rejection should be withdrawn.

The Examiner also contends that the use of "sSNP" and "cSNP" causes the claims to be vague and indefinite. Applicant has presently amended 52, 55, 57, 59, 61 and 63 to recite "single nucleotide polymorphism," which is supported in the specification at pages 249 and 427. As such, the rejection is obviated.

Rejection under 35 U.S.C. §101

Claims 42-47, 49-52, 55, 57, 59, 61, and 63 are rejected under 35 U.S.C.§101. The Examiner alleges that "the claimed invention lacks patentable utility." Applicant respectfully traverses this rejection.

Under 35 U.S.C. §101, Applicant is not required to disclose a "patentable" utility for the invention. What is required is the assertion of a utility that is specific, substantial and credible. Applicant has asserted such a utility for the claimed invention in the specification. For example, in Example 2 beginning at page 265 of the specification, the expression of genes of the invention were assessed quantitatively using microtitre plates containing RNA samples from a variety of

normal and pathology-derived cells, cell lines and tissues by real time quantitative PCR (RTQ PCR). Results for NOV 15b, nucleic acid encoding SEQ ID NO:38, are found in Example 2, section N, pages 391-404. More specifically, Panel 1.3 D results are presented in Table NE at pages 393-396 and summarized on page 403, lines 11-16. A description of the sources of the RNA samples used in Panel 1.3D may be found on page 267. On page 403, lines 11-14, the specification teaches:

> "In addition to expression in brain cancer cell lines, there is substantial expression in other samples derived from cancer cell lines, such as breast cancer, lung cancer, and ovarian cancer. Thus, the expression of this gene could be used to distinguish these samples from other samples in the panel."

Furthermore, Panel 2D includes test samples isolated from human tissue procured by surgeons working in close cooperation with the National Cancer Institute's Cooperative Human Tissue Network (CHTN) or the National Disease Research Initiative (NDRI). Panel 2D results are presented in Table NF at pages 396-400 of the specification and also summarized on page 403, lines 21-31. A description of the sources of the RNA samples used in Panel 2D may be found on page 268. The tissues were derived from human malignancies, and in many cases, normal adjacent tissues (NAT) obtained from non-cancerous tissue just adjacent to the tumor ("matched margins"). The tumor tissue and the "matched margins" were evaluated by two independent pathologists (the surgical pathologists and again by a pathologist at NDRI or CHTN). On page 403, the specification teaches:

> "The highest expression of this gene is generally associated with kidney cancers. Of particular note is the consistent absence of expression in normal kidney tissue adjacent to malignant kidney. In addition, there is substantial expression associated with ovarian cancer, bladder cancer and lung cancer. Thus, the expression of this gene could be used to distinguish the above listed malignant tissue from other tissues in the panel. Particularly, the expression of this gene could be used to distinguish malignant kidney tissue from normal kidney."

One of skill in the art, having read the specification, would therefore know to detect and compare the amount of expression of the nucleotide encoding SEQ ID NO:38 in samples of malignant and normal kidney tissues, by using, e.g. RTQ-PCR methods as described in the specification to differentiate malignant tissues from normal tissues.

The utility described above is specific and substantial. Applicant has not suggested that NOV15b be used in a general undefined way or for diagnosing an unspecified disease. The specification teaches that the nucleic acid encoding the polypeptide of SEQ ID NO:38 may be used as a specific target for detecting expression, particularly in kidney, ovarian, bladder and lung tissue, to differentiate normal tissue from malignant tissue. Furthermore, the specification teaches that not any nucleic acid but specifically NOV15b may be used for this purpose. Since the applicant has made an assertion that the claimed invention is useful for a particular purpose, and such assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility is not proper. Applicants respectfully request the rejection be withdrawn.

Applicant also acknowledges Examiner's assertion that one of skill in the art would have reason to doubt that sequence similarity alone would reasonably support an assertion of utility for the claimed subject matter. However the Examiner's assertion is moot since the specification teaches a utility, as discussed above, for the claimed subject matter which does not rely on sequence homology.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 42-47, 49-52, 55, 57, 59, 61, and 63 are rejected under 35 U.S.C. §112. first paragraph as allegedly containing subject matter whose use is not enabled in the specification.

Applicant respectfully disagrees. As discussed above, the specification clearly describes how to use the claimed invention and provides at least one asserted specific, substantial and credible utility.

As described in the specification, the nucleic acid molecule encoding SEQ ID NO:38 may be used for differentiating malignant tissues from normal tissues, particularly in kidney, ovarian, bladder and lung tissues. For example, the expression of SEQ ID NO:38 may be detected using RTQ-PCR methods as described in the specification, Example 2, to obtain the results described in Section N, pages 391-404, particularly in Table NE at pages 393-396, and

Table NF at pages 396-400. One of skill in the art would appreciate that the expression of the polynucleotide encoding SEQ ID NO:38 is higher in certain malignant tissues compared to normal tissue counterparts, and therefore may be used to aid in differentiating the malignant tissues from normal tissues. Applicant respectfully requests that the rejection be withdrawn.

Claim 45 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter not described in a way so as to convey that the inventors had possession of the claimed invention at the time of filing. Specifically, the Examiner contends that sequences that complement the sequence of SEQ ID NO:37 are not described so as to meet the written description provision of 35 US.C. §112, first paragraph.

Applicant strongly disagrees. It is well understood by those of skill in the art that the complement of a first nucleic acid sequence is a matching nucleic acid sequence in which each base is the matched pair of the base in the corresponding position of the first nucleic acid sequence, the matched pairs being adenine:thymine and guanine:cytosine (See Appendix A, Albert L. Lehninger, Biochemistry, Second Edition, Worth Publishers, Inc. New York, NY, 1979 page 865). Therefore, given the sequence, SEQ ID NO:37, the nucleic acid that is the complement of SEQ ID NO:37 is defined, and can certainly be envisioned by even one of rudimentary skill in the art. Applicant respectfully submits that the rejection should be withdrawn.

Rejection under 35 U.S.C. § 102

Claim 45 is rejected under 35 U.S.C. §102(b) by the Examiner as anticipated by Sigma Catalog product number O 4253, which is *complementary* to the polynucleotide sequence of SEQ ID NO:37 at position 1-3.

Applicant strongly disagrees. While Product No. O 4253 may be "complementary" to SEQ ID NO:37, it is not the complement of SEQ ID NO:37. It is, at best complement of a portion of SEQ ID NO:37. As discussed above, the *complement* of a nucleotide sequence of a specific SEQ ID NO refers to a full length nucleotide sequence comprising the matched base pair at each position of the full length sequence defined by the SEQ ID NO. As such, the subject

matter of claim 45 is clearly not anticipated by Product No. O 4253. Applicant respectfully requests this rejection be withdrawn.

CONCLUSION

Applicant respectfully requests that the amendments and remarks made herein be entered and made of record in the file history of the present application. Applicant respectfully submits that this paper is fully responsive and that the pending claims are in condition for allowance. Such action is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

Janine M. Susan, Reg. No. 46,119
for Ivor R. Elrifi, Reg. No. 39,529

Date: June 4, 2004

Attorney for Applicant
c/o MINTZ, LEVIN
Tel: (617) 542 6000
Fax: (617) 542 2241
Customer No. 30623